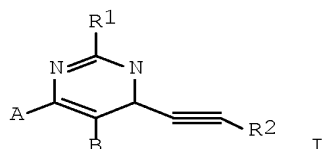


L6 ANSWER 1 OF 1 ZCA COPYRIGHT 2007 ACS on STN
 AN 130:267450 ZCA Full-text
 TI Preparation of ethynylpyrimidine derivatives as tyrosine kinase inhibitors
 and their pharmaceutical uses
 IN Kitano, Yasunori; Kawahara, Eiji; Takayanagi, Hisao; Suzuki, Takeshi;
 Ohya, Atsushi; Hara, Hiroto
 PA Mitsubishi Chemical Industries Ltd., Japan
 SO Jpn. Kokai Tokkyo Koho, 235 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	JP 11080131	A	19990326	JP 1997-251348	19970901 <--
PRAI	JP 1997-251348		19970901		
OS	MARPAT 130:267450				
GI					



AB The derivs. I [A, B = NO₂, (CH₂)_n (n = 0, 1), NR₃R₄ (R₃, R₄ = H, C1-5 alkyl which may be substituted with CO₂H or C1-5 alkoxy carbonyl) or AB = CX₁:CX₂CX₃:CX₄ [X₁-X₄ = H, halo, NO₂, OR (R = C3-8 cycloalkyl which may contain O, C1-5 alkyl which may be substituted with C1-5 alkoxy, amino, morpholino), amino which may be substituted with C1-5 alkyl; neighboring 2 groups of X₁-X₄ may be bonded to each other to be C1-5 oxyalkylene], N: CX₅CX₆:CX₇ (X₅-X₇ = H, halo, C1-5 alkoxy, amino which may be substituted with C1-5 alkyl), CX₈:NCX₉:CX₁₀ (X₈-X₁₀ = any group given for X₅-X₇), N: CX₁₁CX₁₂:N (X₁₁, X₁₂ = H, C1-5 alkyl), W: CX₁₃NX₁₄ (W = N, CX₁₅, X₁₃-X₁₅ = H, C1-5 alkyl), CX₁₆:CX₁₇O (X₁₅, X₁₇ = H, C1-5 alkyl); R₁ = H, halo, (halo)phenyl, C1-5 (phenyl)alkyl, C1-5 alkoxy which may be substituted with CO₂H or C1-5 alkoxy carbonyl, OH, amino which may be substituted with C1-5 alkyl or C1-5 alkanoyl; R₂ = CR₃R₄R₅ [R₃, R₄ = H, halo, pyridyl, pyridazinyl, (C3-8 cycloalkyl)-C1-5 alkyl, etc.]; R₅ = OH, C1-5 alkyl, C1-5 alkoxy carbonyl, C1-5 alkanoyloxy, CO₂H, etc], their hydrates, pharmacol. acceptable salts, optically-active isomers, racemates, and diastereomer mixts. are prepared I are useful for prophylactic and/or therapeutic agents for diseases due to acceleration of tyrosine kinase activity, e.g. as antitumor agents, immunosuppressants, platelet aggregation inhibitors, antiatherosclerotics, inflammation inhibitors, etc. Et₂NCMe₂C.tplbond.CH was treated with EtMgBr and the resulting grignard reagent was treated with 4-chloro-2-phenylquinazoline (preparation given) to give I (R₁ = Ph, R₂ = CMe₂NEt₂, AB = CH:CHCH:CH) (II). This was dissolved in Et₂O and treated with HCl/EtOAc to give II.HCl. IC₅₀ values of this salt against EGF receptor tyrosine kinase activity and growth of human nasopharyngeal carcinoma KB cells were 14 μM and 0.89 μM, resp.